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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,312	04/13/2001	Lisbeth Illum	8567-603US (WESR/P21598US	2569

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 01/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/834,312	ILLUM ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,20,21 and 28-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,21 and 28-39* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Examiner acknowledges receipt of request for continued examination under 37 CFR 1.114, request for extension of time, after final amendment and 131declaration, all filed 10/22/03. Claims 7, 20, 21, 28-39 are pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/22/03 has been entered.

Claim Rejections - 35 USC § 102

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 34 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Carr et al. (US 4,254,129).

Carr discloses a composition comprising 0.01 to 20 mg/kg, of body weight of a patient, of a piperidine derivative of formula I of which fexofenadine is one when R_1 is OH, R_2 is H, R_3 is COOH and n is 3 (abstract, column 1, lines 28-47, column 3, lines 58 and 59), or pharmaceutically acceptable salt (column 3, lines 31-51), and carrier where the carrier can be

propylene glycol or polyethylene glycol (column 5, lines 52-59). Carr discusses administering the composition to warm-blooded animals and representative warm-blooded animals are humans, cats, dogs, bovine cows, lambs and mice and quinea pigs (column 5, line 8 and column 6, lines 1-6); and the administration is by subcutaneous, intramuscular or intravenous administration; or intranasal instillation or topical application to mucous membranes of the nose or throat or bronchial tubes (column 5, lines 8-16). Instant claim 34 is a composition claim and future intended use is not critical in a composition claim. The method of instant claim 20 is directed to administration of the composition of instant claim 34. Carr discloses administering the prior composition to mucous membranes of animals as discussed above. Thus, the teaching of Carr meets the limitations of the claims.

Applicants' argument stating that Carr does not teach fexofenadine has been considered but is not persuasive because Carr teaches fexofenadine as exemplified by formula I when R_1 is OH, R_2 is H, R_3 is COOH and n is 3.

Applicants' argument with respect to Conte and Chiesi are moot in new grounds of rejection.

Claim Rejections - 35 USC § 103

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 30-33, 35 and 37 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Aslanian et al. (US 6,103,735).

Aslanian discloses a composition and method of using the composition to treat allergic rhinitis, asthma and related disorders (abstract, column 1, lines 8-13, column 2, lines 7-24 and 35-41). Aslanian's composition comprises therapeutically effective amount of at least one neurokinin antagonist, therapeutically effective amount of at least one H_3 antagonist and a therapeutically effective amount of at least one H_1 antagonist (column 2, lines 8-24). Fexofenadine is an example of H_1 receptor antagonist (column 5, line 66). Aslanian's composition further comprises carriers, binders, lubricants and disintegrants and examples disclosed in Aslanian are starch, gelatin, sodium alginate, polyethylene glycol, carboxymethylcellulose, sodium benzoate, sodium chloride guar gum, sweetening and flavoring agents (column 6, lines 16-45). Aslanian also discloses that the composition can be formulated as a sustained release product to provide rate-controlled release of one or more of the active agents to optimize the therapeutic effects (column 6, lines 45-48). For liquid formulations, the composition of Aslanian contains propylene glycol in a water-propylene glycol solution (column 6, lines 56-58). Aslanian discloses that a unit dose of the formulation contains 1-200 milligrams of H_1 antagonist or its pharmaceutically acceptable derivative (claims 8-10).

Instant claim 35 requires 100 μg/ml to 100 mg/ml and 0.5% to 40% wt/wt of fexofenadine in the formulation and the comprising language of the instant claim permits the presence of other active agents present in the formulation of the prior art. A unit dose of the prior art is 1-200 mg of fexofenadine H_1 antagonist. However, Aslanian discloses that the actual dosage is dependent on the age of the patient, sex, weight and severity of the condition to be treated (column 7, lines 23-26).

In the event that the unit dose in Aslanian is at least 1 ml, then the concentration of fexofenadine is at least 1 mg/ml to 200 mg/ml and a concentration in the prior art would meet the limitation of one concentration in the instant claim. However, if no concentration of the fexofenadine in the prior art is the same as the concentration of fexofenadine in the instant claim, it is within the purview of one of ordinary skill in the art or the person of skill in the art to adjust the amount of fexofenadine depending on the age of the patient, sex, weight and severity of the condition to be treated according to the disclosure of Aslanian. Also, Aslanian discloses administering the formulation to a patient in need thereof to treat allergic rhinitis, asthma, sneezing, itching runny nose, nasal congestion, redness of the eye, tearing, itching of the ears or palate, wheezing, sinusitis and coughs associated with postnasal drip (column 2, lines 35-41, column 6, lines 9-12 and claim 23). It is examiners position that one method of treating redness of the eye as disclosed by Aslanian is to administer the formulation of Aslanian to the eye in order to treat redness of the eye. Starch is a polysaccharide.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare and administer to a patient in need thereof a unit dose of a formulation that contains fexofenadine in the amount of 1-200 mg/ml, neurokinin antagonist, and at least one H_3 antagonist. One having ordinary skill in the art would have been motivated to adjust the amount of fexofenadine with the expectation that the formulation containing the desired amount of fexofenadine, neurokinin antagonist and at least one H_3 antagonist would effectively treat allergic rhinitis, asthma and related disorders.

6. Claims 30-33, 35 and 37 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hwang et al. (US 6,451,815).

Hwang discloses composition comprising antihistamine of formula I or pharmaceutically acceptable salt, and when R is H, formula I satisfies the structure of fexofenadine (abstract and column 2, lines 20-57). One formulation of Hwang is a combination of fexofenadine and p-glycoprotein inhibitors such as poloxamer (PLURONIC F-68), polyethylene glycol, polyoxyethylene castor (cremophor) and vitamin E (column 8, lines 44, 48, 49, 54-63; column 5, lines 35-41); and the formulation further comprises one or more adjuvants such as water, saline, glycerin and propylene glycols, carriers or excipients such as gelatin, surfactants, microcrystalline cellulose, lubricants, gum tragacanth, starch or lactose, sweetening agents and flavor agents (column 9, lines 35-57, column 10, lines 1-9). The amount of fexofenadine in the formulation is from about 1 mg to 600 mg as a daily dose; Hwang specifically discloses that the amount of fexofenadine that is administered daily is dependent upon the type of disease to be treated, the degree of severity of the disease and the species of patient to be treated (column 5, lines 4-23). Hwang administers its formulation to a patient in need thereof to treat allergic rhinitis, asthma and other respiratory diseases (abstract, column 1, lines 8-14 and column 2, lines 7-24). Hwang's formulation is administered as capsule, tablet, liquid and suspension (62-67).

Instant claim 35 requires 100 μg/ml to 100 mg/ml and 0.5% to 40% wt/wt of fexofenadine in the formulation and the comprising language allows for the presence of other ingredients that are present in the prior art. Hwang discloses a formulation that contains 1 mg to 600 mg fexofenadine as a daily dose. While instant claim is directed to concentration of the fexofenadine and the prior art discloses amount of the fexofenadine that can be administered daily. If the formulation is administered as ml suspension, the concentration administered as mg/ml in the prior art will coincide with one point on the concentration line of the instant claim.

However, if no concentration of the fexofenadine in the prior art is the same as the concentration of fexofenadine in the instant claim, it is within the purview of one of ordinary skill in the art or the person of skill in the art to adjust the amount of fexofenadine since the amount of fexofenadine that is administered daily is dependent upon the type of disease to be treated, the degree of severity of the disease and the species of patient to be treated according to Hwang.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare and administer to a patient in need thereof a daily dose of a formulation that contains fexofenadine in the amount of 1-600 mg/ml and p-glycoprotein inhibitors such as poloxamer. One having ordinary skill in the art would have been motivated to adjust the amount of fexofenadine with the expectation that the formulation containing the desired amount of fexofenadine, p-glycoprotein inhibitors such as poloxamer and carriers or excipients or binders would effectively treat allergic rhinitis, asthma and related disorders.

7. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carr et al. (US 4,254,129) in view of Hwang et al. (US 6,451,815).

Carr discloses administering a composition comprising fexofenadine to a subject in need thereof by intranasal instillation or topical application to mucous membranes of the nose or throat or bronchial tubes as discussed above. However, Carr is silent on treating rhinitis. However, Hwang discloses a method of treating rhinitis with a fexofenadine (abstract, column 1, lines 8-14 and column 2, lines 7-24). Hwang is relied upon for a teaching of treating rhinitis with fexofenadine.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the formulation of Carr to a subject in need thereof by

intranasal instillation or topical application to mucous membranes of the nose or throat or bronchial tubes. One having ordinary skill in the art would have been motivated to administer the fexofenadine formulation with the expectation of treating rhinitis because it is fexofenadine is known in the prior art (Hwang) to be effective in treating rhinitis.

8. Claims 28, 29, 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carr et al. (US 4,254,129) in view of Hwang et al. (US 6,451,815).

Carr teaches the instant fexofenadine composition except that Carr's composition does not have a gelling agent of bioadhesive. However, Hwang teaches a fexofenadine formulation that contains gelling agent of bioadhesive agent where the gelling agent or bioadhesive of Hwang is poloxamer or starch polysaccharide (column 9, lines 35-57, column 10, lines 1-9, column 8, lines 44, 48, 49, 54-63; column 5, lines 35-41). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the fexofenadine formulation of Carr. One having ordinary skill in the art would have been motivated to include the poloxamer of Hwang with the expectation of enhancing the bioavailability of fexofenadine.

9. Claims 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US 6,267,985).

Chen discloses a pharmaceutical composition that comprises fexofenadine (column 29, line 67) and cyclodextrins or cyclodextrin derivative such as hydroxypropyl cyclodextrin (column 34, lines 6 and 7, claims 50 and 53). Regarding instant claim 36 where the cyclodextrin is hydroxypropyl-β-cyclodextrin, it is noted that the hydroxypropylcyclodextrin of the prior art is a racemic mixture of the hydroxypropyl-β-cyclodextrin and hydroxypropyl-α-cyclodextrin. It is expected that any of the isomers, hydroxypropyl-β-cyclodextrin or

hydroxypropyl-α-cyclodextrin would solubilize the fexofenadine except there is evidence to the contrary that the alpha- or the racemic mixture would not solubilize the fexofenadine.

Chen fails to teach specific amounts of therapeutic agent but discloses that the amount of the therapeutic agent is a maximum amount of the therapeutic agent that can be solubilized in the composition (column 33, lines 39-40). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the composition of Chen. One having ordinary skill in the art would have been motivated to use a maximum amount of fexofenadine in the composition with the expectation that the fexofenadine will be solubilized by the cyclodextrin or its derivative thereof.

10. Claim 7 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims because the prior art dose not teach a composition that consists essentially of fexofenadine and cyclodextrin or hydroxypropyl-β-cyclodextrin.

Observation:

Claim 25 recites the amounts of fexofenadine in μg/ml or mg/ml and percent wt/wt. It is respectfully suggested that the amounts fexofenadine be expressed either as μg/ml, mg/ml or percent wt/wt.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is 571-242-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Blessing Fubara
Patent Examiner
Tech. Center 1600